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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,516	02/11/2005	Hans Loibner	4518-0109PUS1	1154

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EXAMINER	
SANG, HONG	
ART UNIT	**PAPER NUMBER**
1643	

NOTIFICATION DATE	DELIVERY MODE
11/06/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/524,516	LOIBNER ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *6,9-22 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,8 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Loibner et al.

1. Applicants' response filed on 9/10/07 is acknowledged. Claims 1-24 are pending. New claim 24 is added. Claims 6, 9-22, and new claim 24 are withdrawn from consideration as being drawn to non-elected inventions.

Election/Restrictions

2. Applicants' traverse of the restriction requirement is acknowledged. Applicants are reminded that the decision for the restriction has been made final in the previous office action.

After a final requirement for restriction, the applicant, in addition to making any reply due on the remainder of the action, may petition the Director to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested (see 37 CFR1.144.).

Information Disclosure Statement

3. The information disclosure statement (IDS) filed on 9/10/07 has been considered. A signed copy is attached hereto.

4. Claim 1-5, 7, 8, and 23 are under examination. Due to restriction/species election, claims are examined to the extent wherein antigen (a) is EpCAM and antigen (b) is Lewis Y.

Objections Maintained

5. The objection to claims 1-5, 7, 8 and 23 because the claims contain non-elected inventions such as antibody, non-elected antigens NCAM, CEA, Lewis b, sialyl-Tn, and Globe H is maintained.

The response states that applicants will amend the generic claim following an indication of allowability of the elected species.

Because applicants have taken no action, the objection is maintained.

Applicants are reminded that election of (a) EpCAM and (b) Lewis y is a restriction requirement and not a species election.

Response to Arguments

Claim Rejections - 35 USC § 103

6. The rejection of claims 1-5, 7, 8 and 23 under 35 U.S.C. 103(a) as being unpatentable over WO 01/35989A2 (Pub. Date: 5/25/2001, IDS) (English translation CA 2391927) in view of Maruyama et al. (Cancer Immunol Immunother., 2000, 49: 123-132), Sabbatini et al. (Int. J. Cancer, 2000, 87: 79-85), and Berthelsen et al. (US Patent No. 6,455,290B1, Date of Patent 9/24/2002, effective filing date 7/9/1999) is maintained.

The response states that the antigens are significantly different over structures, which only mimic such an antigen epitope. The response states that although WO 01/35989 discloses the purified preparation of an EpCAM and Lewis Y anti-idiotypic antibody, it actually does not suggest the use of a combination, over the improved results achieved by use of such a combination. The combined preparation of EpCAM

and Lewis Y antibodies according to WO 01/35989 cannot simply be adapted to a combined pharmaceutical preparation of antigens. When using antigens, the lower specificity and higher (unspecific) immunogenicity has to be considered. A host challenged with an antigen will suffer from an increased and more severe immune reaction in combination to a challenge with an anti-idiotypic antibody. This effect is further potentiated by the combined use of two antigens and thus the presented inventive combination does not appear recommended in view of the state of the art. The response states that the use of an antigen in a therapy can be problematic over the use of anti-idiotypic antibody. Luo's and Kieber-Emmons's references argue that carbohydrate Lewis Y (LeY) is generally problematic for induction of a T-cell dependent immune response, and consequently the use of peptide/protein mimics (including anti-idiotypic antibodies) would be the primarily preferred way to go based on the state of the art. Maruyama et al. describes a study where it was reported that the anti-idiotypic antibodies mimicking a bacterial antigen primed protection whereas the antigen itself did not (s. Maruyama et al., p. 130, 2nd paragraph). Therefore, there are several reasons which would discourage the skilled man in the art, or at least provide no incentive, for trying to prepare a combined vaccine with EpCAM and Lewis Y antigens in particular - or generally according to claim 1 of the present application.

Applicant's arguments have been carefully considered but are not persuasive. Luo's and Kieber-Emmons's references are insufficient to overcome the instant rejection. Although a host challenged with an antigen may suffer from an increased and more severe immune reaction, both EpCAM antigen and Lewis y antigens have been

used successfully in the prior art as a vaccine for treating cancer. Maruyama et al. teach a cancer vaccine comprising the antigen GA733 (EpCAM). Sabbatini et al. teach a vaccine comprising Lewis y antigen for treating ovarian cancer (see abstract). While neither Maruyama nor Sabbatini teaches a vaccine comprising both EpCAM and Lewis y antigens, the use of these two antigens together is obvious in view of the teachings of WO 01/35989A2. WO 01/35989A2 teaches a pharmaceutical composition (vaccine) comprising anti-idiotypic antibody for EpCAM, anti-idiotypic antibody for Lewis Y, or anti-idiotypic antibodies for both EpCAM and Lewis Y antigens (see page 7, Examples 1-7, and claim 16). WO 01/35989A2 teaches that within an immunologic meaning, some anti-idiotypic antibodies can represent the "internal image" of an antigen, such antibodies may therefore be used, as a vaccine, for inducing an immune response in cancer patients, said immune response being possibly directed against said tumor-associated antigen (see page 2, 3rd paragraph and page 3, lines 3-6 of CA 2391927). Therefore, WO 01/35989A2 teaches that antigenic mimics of EpCAM and Lewis y can be used together for treating cancer. In view of the teachings of WO 01/35989A2, Maruyama and Sabbatini, one skilled in the art would expect that EpCAM and Lewis y antigens can be used together for treating cancer given the fact that they induce immune response to the same proteins i.e. EpCAM and Lewis y as their anti-idiotypic antibodies do. Furthermore, Maruyama et al. teach that the immunomodulatory activity of the native antigen GA733 (EpCAM) is superior to that of the anti-idiotypic antibody (Ab2) which mimicking a single EpCAM epitope (see abstract). One would have been motivated to use the native antigen GA733 instead of its anti-idiotypic antibody. One of

ordinary skill in the art would have a reasonable expectation of success to make the vaccine of GA733 and Lewis y antigen because each of the antigens is known in the art and has been prepared as a cancer vaccine.

Regarding applicant's argument that that Maruyama et al. describes a study where the anti-idiotypic antibodies mimicking a bacterial antigen primed protection whereas the antigen itself did not (s. Maruyama et al., p. 130, 2nd paragraph), this is not persuasive because the antigen is not the claimed EpCAM. Moreover, Maruyama et al. explicitly disclose that the immunomodulatory activity of the native antigen GA733 (EpCAM) is superior to that of the anti-idiotypic antibody (Ab2) which mimicking a single EpCAM epitope (see abstract).

In response to applicant's argument that the column 20, lines 45-61 of Berthelsen' reference does not disclose the method of making intravenously tolerable preparation comprising antibodies or polypeptides, this argument is not persuasive. As indicated in the previous office action, the method of making intravenous tolerable preparation comprising antibodies is known in the art, as evidence by Berthelsen. Berthelsen discloses that the pharmaceutical composition comprising antibodies identified by the screening methods can be prepared for any route of administration including intravenous (see particularly lines 51, and 54).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made.

7. The rejection of claims 1-5, 7, 8 and 23 under 35 U.S.C. 103(a) as being unpatentable over Spitler (US Patent NO. 5,738,867, 4/14/1998) in view of Sabbatini et al. (Int. J. Cancer, 2000, 87: 79-85), and Berthelsen et al. (US Patent No. 6,455,290B1, Date of Patent 9/24/2002, effective filing date 7/9/1999) is maintained.

The response states that Spitler describes an anti-tumor preparation with an antigen or anti-idiotypic antibody in a liposome preparation. Claim 2 of Spitler mentions that in the anti-tumor vaccine an "additional synthetically prepared tumor associated antigen" can be present. However, the assertion of an expected synergistic effect is completely unfounded and pure hindsight. When using two antigens in one preparation it is expected that - if those antigens do not negatively interfere with each other's functionality - at best each antigen would result in its own single effect and the sum of those effects could be observed. However, a synergistic effect requires that the observed effect would be increased as compared to the sum of each single effect of the antigens. Such an increased effect is shown by the examples in the present application and is completely surprising and inventive over the state of the art.

Applicant's arguments have been carefully considered but are not persuasive. The use of a vaccine comprising two or more tumor-associated antigens is well known in the art, as shown by the teaching of Spitler. Spitler teaches that the antitumor vaccine compounds may be employed in cocktails of two or more different TAAs encapsulated in and/or conjugated to liposomes, and such cocktails may be of particular in certain highly metastatic cancers (see the paragraph bridging columns 4 and 5). Spitler teaches an antitumor vaccine composition comprising a GS-733-2 antigen

(EpCAM) in a liposomal carrier (see abstract and claim 1) for treatment of cancer including ovary cancer (see column 2, lines 24-27). Sabbatini et al. teach a vaccine comprising Lewis y antigen for treating ovarian cancer (see abstract). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a vaccine comprising EpCAM and Lewis Y antigens in view of the teachings of Spitler, and Sabbatini et al. One would have been motivated to do so because both EpCAM antigen and Lewis y antigen are used to treat ovarian cancer. Furthermore, Spitler teaches that the vaccine of EpCAM can further comprise additional tumor associated antigen. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Even if the combination of EpCAM and Lewis y antigens does not provide synergistic effect (which applicants failed to provide evidence), the combination of the drugs that possesses the therapeutic effects of each individual drug would still provide motivation to one skilled in the art because the combination is at least more effective than the single drug. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Rejections Withdrawn

8. All other rejections are withdrawn in view of applicant's amendment to the claims or persuasive arguments.

Conclusion

9. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
October 11, 2007

/Christopher Yaen/
Primary Examiner
Art Unit 1643
October 25,2007